Effect of EGCG on granule cell proliferation in the adult dentate gyrus of the Ts65Dn mouse

Zahir Sheikh, Charles Goodlett
Department of Psychology, IUPUI School of Science

Down syndrome (DS) is the most common genetic disorder that results in cognitive abnormalities and occurs in approximately 1 in 700 live births. This disorder is caused by an extra copy of human chromosome 21 (Hsa21) which increases the dosage of the genes on that chromosome. Ts65Dn mice, which are the most studied mouse model for DS, are trisomic for segments of mouse chromosome 16 (Mmu16) which contain approximately half the genes found on Hsa21. These mice express some of the physical and behavioral abnormalities associated with DS. Previous research has shown impaired performance of Ts65Dn mice in hippocampal-dependent tasks, such as in the radial arm maze task, compared to euploid control mice. Success in such tasks is thought to depend on the ability of the hippocampus to generate granule cells within the dentate gyrus. Young granule cells are highly active after integration and are required for memory formation. Previous research shows that Ts65Dn have a reduction in the formation of granule cells which leads us to hypothesize that Ts65Dn mice will perform worse in the radial arm maze compared to euploid controls. This leads us to conclude that Ts65Dn mice have reduced granule cell proliferation relative to controls. We are investigating the effects of EGCG, a polyphenolic component of green tea, on granule cell proliferation in adult mice. Different pathways are suggested to be effected by EGCG, such as by inhibiting Dyrk1a that is overproduced in DS mice or by up-regulation of the sonic hedgehog receptor Patched. Using BrdU peroxidase immunohistochemistry to label newly generated granule cells in the adult mouse dentate gyrus, we hypothesize that EGCG will increase cell proliferation in the granule cell layer of the dentate gyrus.

Mentor: Charles Goodlett, Department of Psychology; IUPUI School of Science; IUPUI; Indianapolis, IN